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A New Shock Model for the Effect of Leptin on Body Weight Gain

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Abstract
The present study was designed to examine the dosage effect of the chronic Leptin infusion on body weight gain. Using a new shock model approach, the mean and variance for body weight gain were found. The results are consistent and the shock model concludes that if the dosage of the Leptin increases, the body weight gain decreases.
Keywords: New Shock model, Leptin, neuroendocrine, neuropeptides.
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1. Introduction

Shock models provide a realistic formulation for modeling certain reliability system situated in a random environment. Rade [1] and Nakagawa [2] considered a parallel system which is subject to shocks that occurs according to a renewal process. Consider a system subjected to shocks occurring randomly in time. Each shock causes damage and the damage accumulates. The system fails when the total accumulated damage exceeds a certain threshold level.

Leptin plays a major role in energy homeostasis. Leptin acts on precise populations of hypothalamic neurons to normalize feeding behavior, energy expenditure and neuroendocrine function. Increasing Leptin levels are proposed to limit weight gain through inhibition of food intake and increased thermogenisis[5], [6]. A second aspect of Leptin action occurs as levels fall with hunger, triggering metabolic and neuroendocrine responses that reduce energy expenditure and promote feeding behavior [7], [8]. Leptin influences both of these aspects of energy homeostasis mostly by regulating the expression of hypothalamic neuropeptides, which then influence feeding behavior, autonomic and neuroendocrine function.

Dosage of Leptin infusion is taken as a shock and if the Leptin infusion level exceeds a threshold level, which is assumed to be a discrete random variable then the system reaches the failure state. Here the failure state is considered as the body weight gain.

2. Notations

Z	–	random variable denoting the time between two successive shocks
f(.), F(.)	–	Probability density, Cumulative distribution functions of Z.
D	–	random variable denoting the threshold value.
λ	–	scale parameter of exponential distribution
g(.), G(.)	–	Probability density, cumulative distribution functions of D.
W	–	Random variable denoting time between two successive failures.
k(t), K(t)	–	Probability density, Cumulative distribution functions of W.
$L_f(s)$	–	Laplace transform of the function f(t).

3. Assumptions of the stochastic model

1. A well being is exposed with a number of shocks which leads to stress.
2. The interval between shocks Z, are assumed to be independently and identically distributed random variable with distribution function F(.)
3. A shock is classified as a non lethal shock if the time elapsed from the previous shock to this shock is greater than the threshold D. A shock is lethal if it occurs within D. A lethal shock results in system failure leading to stress related deficit symptoms.
4. Threshold time D is a random variable with distribution function G(.).
5. The shock arrival times and the threshold time are independent of each other.

4. A New Shock model

Shocks are events which cause perturbation to the system, leading to its deterioration and consequent failure. Here we assume that the infusion of chronic Leptin dosage is considered as shock. The effect of these shocks is measured by a process called wear process or damage process. Interesting variations of the first passage problem have been studied by Shanthi kumar and Sumitha [3], Stadje[4], Y. Lam and Zhang [9]. The shock that leads to the threshold crossing is known as lethal shock, we are led to the fact that W, the time between two successive

failures comprises the number of intervals, each of which is greater than D and one interval whose length is less than D. We observe that W can be represented as the sum of a random number of random variables, so that,

$$W = \sum_{i=1}^{N-1} X_i + Y_N$$

The number of terms N-1 in the summation is a random variable representing the number of non lethal shocks experienced by the system during one cycle. From our assumptions; it is immediate that N has the geometric distribution given by

$$P[N = n] = qp^n,\ n=0,1,2\ldots \quad \text{where } q = P[Z \le D] \text{ and } p = 1-q.$$

Define the conditional distributions of X_i and Y_N as

$$\alpha(x) = P[x < z < x + dx / Z > D] = \frac{f(x)G(x)}{P(z > D)} \text{ and}$$

$$\beta(x) = P[x < z < x + dx / z \le D] = \frac{f(x)\,\overline{G}(x)}{P(z \le D)}$$

Now,

$$K(t) = P[t \le W \le t + dt]$$

$$= \sum_{n=0}^{\infty} P[t \le W \le t + dt / N = n].P(N = n)$$

$$= \sum_{n=0}^{\infty} [\alpha^{(n)} * \beta(t)]\, P(z \le D)\, [P(z > D)]^n \qquad \text{----------} \rightarrow (1)$$

Where $\alpha^{(n)} * \beta(t)$ is the convolution of the n fold convolution of $\alpha(t)$ and $\beta(t)$.
Taking the Laplace transform on both sides of (1), we get

$$L_k(S) = \frac{L_f\,\overline{G}(S)}{1 - L_f\,G(S)}$$

The moments of W for any shock arrival distribution f (t) are simply obtained by differentiating $L_k(S)$ successively and setting S = 0.

The mean and variance of W is

$$E[w] = \frac{E(z)}{P(z \le D)}$$

$$Var[w] = \frac{E(Z^2)}{P(Z \le D)} + \frac{2E(Z)\,E(Z / Z > D)\,P(Z > D) - E^2(Z)}{P(z \le D)^2}$$

When the system is subjected to the same kind of shock each time, the threshold time of the system is likely to remain a constant, a case discussed by Yeh Lam[9]. Under such a Scenario, We consider a model for different shock arrival distributions. We assume the shock arrivals are according to an exponential density with mean $\frac{1}{\lambda}$. The relevant statistical characteristics can be derived as

$$K(t) = \lambda e^{-\lambda t} \sum_{n=0}^{\infty} \frac{\lambda^n}{n!} \left\{ (t - nD)^n u_{nD} - [t - (n+1)D]^n u_{(n+1)D} \right\}$$

where u_α is the Heaviside unit step function defined as

$$u_\alpha(t) = \begin{cases} 1, & t \ge \alpha \\ 0, & t < \alpha \end{cases}$$

Then

$$E[W] = \frac{1}{\lambda(1 - e^{-\lambda D})}$$

$$Var[W] = \frac{2(1 - e^{-\lambda D}) + 2\lambda e^{-\lambda D}(\lambda D e^{-\lambda D} - e^{-\lambda D})}{\lambda^2 (1 - e^{-\lambda D})^2}$$

$$= \frac{2(1 - e^{-\lambda D}) + 2\lambda e^{-2\lambda D}(\lambda D - 1)}{\lambda^2 (1 - e^{-\lambda D})^2}$$

5. Application

Let us consider an example to measure the body weight during the light and dark cycles on successive days in three groups of rats each of 5 per group. Leptin was infused at a rate of 2 mg/h and 4 mg/h in two groups of rats and saline was infused to the control group (i.e.vehicle). From Fig. 1., it was observed that the body weight gain was not affected considerably within the first 3 days of Leptin infusion, but it decreased afterward. A dose effect of Leptin to reduce weight gain was observed after the infusion and persisted through the period of the experiment.

The scale parameter for the vehicle control is measured as $\lambda = 0.0034$. For 2mg /h of Leptin infusion the scale parameter is $\lambda = 0.0036$ and to 4 mg /h of Leptin infusion the scale parameter is $\lambda = 0.0038$. For the threshold value D = 1, the expected time and variance of the body weight gain for the control group rats and for the infusion of 2mg /h and 4 mg/h of Leptin by using the shock model were calculated and is given in Fig. 2., and Fig. .3.

6. Conclusion

Using the new shock model approach, the mean and variance for the body weight gain were found. The results are consistent and the shock model concludes that if the value of λ increases then the mean and variance are decreased. This indicates that the differential effect of the dosage of the Leptin increases, the body weight gain decreases.

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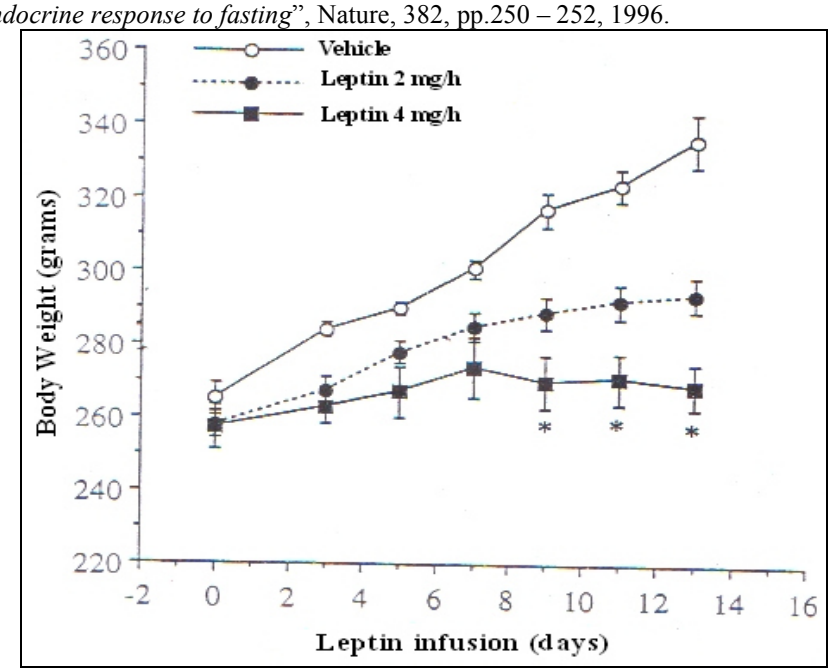

Fig. 1. Dose effect of chronic Leptin infusion on body weight gain

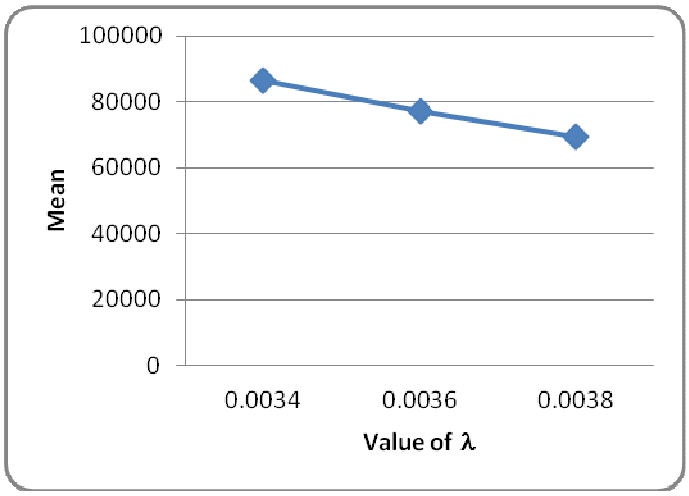

Fig. 2. The mean for the body weight gain

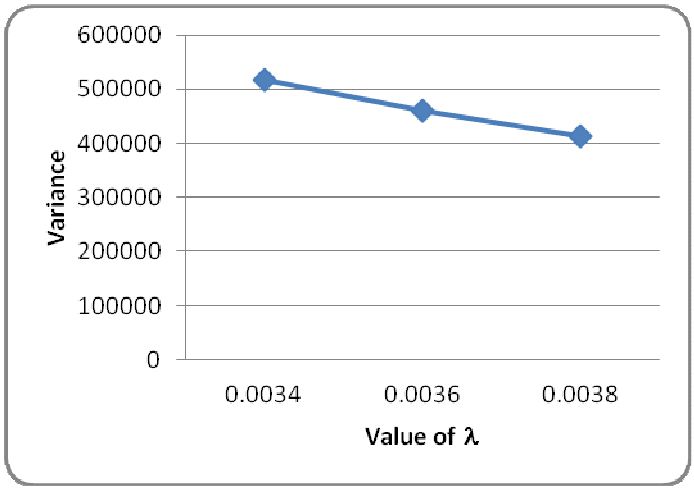

Fig. 3. The variance for the body weight gain

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